SAFETY DATA SHEET
Rizatriptan Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Rizatriptan Formulation

Manufacturer or supplier's details
Company name of supplier: Organon & Co.
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone: 52 55 57284444
Emergency telephone: 215-631-6999
E-mail address: EHSSTEWARD@organon.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure (Oral): Category 1 (Cardio-vascular system)

GHS label elements
Hazard pictograms:

Signal Word: Danger
Hazard Statements: H361d Suspected of damaging the unborn child.
H372 Causes damage to organs (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

Precautionary Statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Storage:
P405 Store locked up.

Disposal:
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P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 50 -&lt; 70</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 -&lt; 20</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td>&gt;= 5 -&lt; 10</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

If inhaled
If inhaled, remove to fresh air.
Get medical attention.

In case of skin contact
In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact
If in eyes, rinse well with water.
Get medical attention if irritation develops and persists.

If swallowed
If swallowed, DO NOT induce vomiting.
Get medical attention.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed
Suspected of damaging the unborn child.
Causes damage to organs through prolonged or repeated exposure if swallowed.
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.

Protection of first-aiders
First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician
Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media : Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
**SECTION 6. ACCIDENTAL RELEASE MEASURES**

**Personal precautions, protective equipment and emergency procedures**
- Use personal protective equipment.
- Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

**Environmental precautions**
- Avoid release to the environment.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spills cannot be contained.

**Methods and materials for containment and cleaning up**
- Sweep up or vacuum up spillage and collect in suitable container for disposal.
- Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air).
- Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration.
- Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
- Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

**SECTION 7. HANDLING AND STORAGE**

**Technical measures**
- Static electricity may accumulate and ignite suspended dust causing an explosion.
- Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

**Local/Total ventilation**
- Use only with adequate ventilation.

**Advice on safe handling**
- Do not breathe dust.
Do not swallow.
Avoid contact with eyes.
Avoid prolonged or repeated contact with skin.
Wash skin thoroughly after handling.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment
Minimize dust generation and accumulation.
Keep container closed when not in use.
Keep away from heat and sources of ignition.
Take precautionary measures against static discharges.
Do not eat, drink or smoke when using this product.
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures:
If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place.
When using do not eat, drink or smoke.
Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

Conditions for safe storage:
Keep in properly labeled containers.
Store locked up.
Store in accordance with the particular national regulations.

Materials to avoid:
Do not store with the following product types:
Strong oxidizing agents
Organic peroxides
Explosives
Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
Containment technologies suitable for controlling compounds
are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

### Personal protective equipment

**Respiratory protection**: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

- **Filter type**: Particulates type

**Hand protection**: Material: Chemical-resistant gloves

**Remarks**: Consider double gloving.

**Eye protection**: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

**Skin and body protection**: Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: pink
- **Odor**: odorless
- **Odor Threshold**: No data available
- **pH**: No data available
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: Not applicable
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: May form explosive dust-air mixture during processing, handling or other means.
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper**: No data available
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flammability limit
Lower explosion limit / Lower flammability limit: No data available
Vapor pressure: No data available
Relative vapor density: No data available
Density: No data available
Solubility(ies)
  Water solubility: No data available
Partition coefficient: n-octanol/water: No data available
Autoignition temperature: No data available
Decomposition temperature: No data available
Viscosity
  Viscosity, kinematic: No data available
Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: No data available
Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY
Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions
  May form explosive dust-air mixture during processing, handling or other means.
  Can react with strong oxidizing agents.
Conditions to avoid
  Heat, flames and sparks.
  Avoid dust formation.
Incompatible materials
  Oxidizing agents
Hazardous decomposition products
  No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure
Inhalation
Skin contact
Ingestion
Eye contact
Acute toxicity
Not classified based on available information.

**Product:**

Acute oral toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

**Components:**

**Cellulose:**

Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg

Acute inhalation toxicity : LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist

Acute dermal toxicity : LD50 (Rabbit): > 2,000 mg/kg

**Starch:**

Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg

Acute dermal toxicity : LD50 (Rabbit): > 2,000 mg/kg

**Rizatriptan:**

Acute oral toxicity : LD50 (Rat): 2,227 mg/kg
  LD50 (Mouse): 700 - 1,631 mg/kg

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Rizatriptan:**

Species : Rabbit
Result : No skin irritation

**Serious eye damage/eye irritation**
Not classified based on available information.

**Components:**

**Starch:**

Species : Rabbit
Result : No eye irritation

**Rizatriptan:**

Species : Bovine cornea
Remarks : Moderate eye irritation
Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Starch:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Result: negative

Rizatriptan:
Test Type: Maximization Test
Routes of exposure: Dermal
Species: Guinea pig
Assessment: Does not cause skin sensitization.
Result: negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Genotoxicity in vivo:
Test Type: In vitro mammalian cell gene mutation test
Result: negative

Starch:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Rizatriptan:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

Test Type: Alkaline elution assay
Result: negative

Test Type: In vitro mammalian cell gene mutation test
Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative

Genotoxicity in vivo:
Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
Species: Mouse
Application Route: Oral
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Cellulose:
Species: Rat
Application Route: Ingestion
Exposure time: 72 weeks
Result: negative

Rizatriptan:
Species: Mouse
Application Route: Oral
Exposure time: 100 weeks
NOAEL: 125 mg/kg body weight
Result: negative
Species: Rat
Application Route: Oral
Exposure time: 106 weeks
NOAEL: 106 mg/kg body weight
Result: negative

Reproductive toxicity
Suspected of damaging the unborn child.

Components:

Cellulose:
Effects on fertility:
Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Result: negative

Effects on fetal development:
Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

Rizatriptan:
Effects on fertility:
Test Type: Fertility/early embryonic development
Species: Rat, female  
Application Route: Oral  
Fertility: LOAEL: 100 mg/kg body weight  
Symptoms: altered estrus cycles  
Result: No effects on fertility and early embryonic development were detected.

Test Type: Fertility/early embryonic development  
Species: Rat, male  
Application Route: Oral  
Fertility: NOAEL: 250 mg/kg body weight  
Result: No effects on fertility and early embryonic development were detected.

Effects on fetal development:
Test Type: Embryo-fetal development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: LOAEL: 10 mg/kg body weight  
Result: No teratogenic effects., Embryo-fetal toxicity.

Test Type: Embryo-fetal development  
Species: Rabbit  
Application Route: Oral  
Developmental Toxicity: LOAEL: 100 mg/kg body weight  
Result: No teratogenic effects., Embryo-fetal toxicity.  
Remarks: The effects were seen only at maternally toxic doses.

Reproductive toxicity - Assessment:  
Some evidence of adverse effects on development, based on animal experiments.

**STOT-single exposure**
Not classified based on available information.

**Components:**

**Rizatriptan:**
Assessment: May cause drowsiness or dizziness.

**STOT-repeated exposure**
Causes damage to organs (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

**Components:**

**Rizatriptan:**
Target Organs: Cardio-vascular system  
Assessment: Causes damage to organs through prolonged or repeated exposure.
Repeated dose toxicity

Components:

Cellulose:
Species: Rat
NOAEL: >= 9,000 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Starch:
Species: Rat
NOAEL: >= 2,000 mg/kg
Application Route: Skin contact
Exposure time: 28 Days
Method: OECD Test Guideline 410

Rizatriptan:
Species: Rat
LOAEL: 1 mg/kg
Application Route: Oral
Exposure time: 14 Weeks
Symptoms: Dilatation of the pupil, Increased pulse rate, Redness

Species: Dog
LOAEL: 0.05 mg/kg
Application Route: Intravenous
Exposure time: 2 Weeks
Symptoms: Dilatation of the pupil, Increased pulse rate, Redness

Species: Dog
LOAEL: 0.2 mg/kg
Application Route: Oral
Exposure time: 1 y
Symptoms: Dilatation of the pupil

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Rizatriptan:
Ingestion: Target Organs: Cardio-vascular system
Symptoms: asthenia, Fatigue, Pain, Dizziness, Weakness, Drowsiness
Ecotoxicity

**Components:**

**Cellulose:**
- Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l  
  Exposure time: 48 h  
  Remarks: Based on data from similar materials

**Rizatriptan:**
- Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 1,000 mg/l  
  Exposure time: 96 h
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 1,000 mg/l  
  Exposure time: 48 h
- Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201  
  NOEC (Pseudokirchneriella subcapitata (green algae)): 48 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201
- Toxicity to fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 9.6 mg/l  
  Exposure time: 32 d  
  Method: OECD Test Guideline 210
- Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 110 mg/l  
  Exposure time: 21 d  
  Method: OECD Test Guideline 211
- Toxicity to microorganisms: EC50: > 1,000 mg/l  
  Exposure time: 3 h  
  Test Type: Respiration inhibition  
  Method: OECD Test Guideline 209  
  NOEC: 1,000 mg/l  
  Exposure time: 3 h  
  Test Type: Respiration inhibition  
  Method: OECD Test Guideline 209

**Persistence and degradability**

**Components:**

**Cellulose:**
- Biodegradability: Result: Readily biodegradable.
Rizatriptan:

Biodegradability :
Result: Not readily biodegradable.
Biodegradation: 50 %
Exposure time: 13 d
Method: OECD Test Guideline 314

Bioaccumulative potential

Components:

Rizatriptan:
Partition coefficient: n-octanol/water :
log Pow: -0.649

Mobility in soil

Components:

Rizatriptan:
Distribution among environmental compartments :
log Koc: 3.83
Method: OECD Test Guideline 106

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues :
Dispose of in accordance with local regulations.
Contaminated packaging :
Empty containers should be taken to an approved waste handling site for recycling or disposal.
If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

Domestic regulation

NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable
SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.

The ingredients of this product are reported in the following inventories:

- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- ACGIH / TWA: 8-hour, time-weighted average
- NOM-010-STPS-2014 / VLE-PPT: Time weighted average limit value

All abbreviations are explained in the text of the document.
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The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8